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used to identify risk factors for the development of death from VAP. **Results:** A total of 73,215 admissions complicated by VAP were identified during the study period with 59,158 survivors and 14,057 non-survivors, yielding a death rate of 19.2%. A significant portion of patients had 3 or more comorbid conditions (41.4%). The most frequent comorbid conditions reported by patients in the cohort were hypertension (42.5%), congestive heart failure (23.9%), and diabetes (23.1%). Multivariate regression identified the following significant risk factors for death: admission diagnosis of sepsis (aOR 2.48, 95% CI 2.24–2.73), history of malignancy (aOR 2.17, 95% CI 1.80–2.62), age >65 years (aOR 1.80, 95% CI 1.62–2.01), history of liver disease (aOR 1.61, 95% CI 1.34–1.94), and renal failure (aOR 1.55, 95% CI 1.33–1.82). Gender, race, and hospital region/type/size were not associated with the risk of death. The death rate for patients with zero chronic conditions was 11.3%. Each additional chronic condition was associated with an increase in risk of death of 5% (aOR 1.05, 95% CI 1.03–1.07). **Conclusions:** Significant risk factors for death include age >65 years, history of malignancy, pre-existing liver disease, renal failure, and sepsis. The risk of death increases with each additional comorbid conditions. There was no effect of reporting facility demographics on risk of death.

## 681

### NONINVASIVELY DETERMINED WORK OF BREATHING DURING NONINVASIVE PRESSURE SUPPORT: VALIDATION STUDY

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**Learning Objectives:** We describe a computerized method of making real-time corrections of tidal volume (VT) in the presence of facemask leaks during non-invasive pressure support (PS) with expiratory positive airway pressure (EPAP)1 so that real-time, noninvasively determined work of breathing/minute (WOBN/min) may be estimated using artificial neural network software (ANN).2 We hypothesized that valid estimations of WOB may be obtained using this method. To test this hypothesis, we performed a validation study. **Methods:** With IRB and informed consent, healthy adult volunteers (n = 8, 8 males, 187 ± 23 lb, 38 ± 8 years) received noninvasive PS ranging from 3–10 cm H2O combined with EPAP ranging from 4–5 cm H2O (V60, Respirationics). A combined pressure/flow sensor, placed between the facemask and the end of the ventilator breathing tubing, directed data to a respiratory monitor (NM3, Respirationics) and a laptop computer containing the VT leak-correction algorithm software and WOBN/min and ANN software (Convergent Engineering).2 Changes in esophageal pressure (Pes) from a catheter in the esophagus were integrated with changes in VT, obtained from the VT leak-correction algorithm, to form a Pes VT loop that, in turn, was applied to a Campbell diagram for determination of physiologic WOB per minute (WOBPHYS/min), i.e., the actual WOB. The same VT as obtained from the VT leak correction algorithm used in determining WOBPHYS/min was also used for WOBN/min. Data were analyzed with regression and Bland-Altman analyses; alpha was set at 0.05 for statistical significance. – **Results:** VT ranged from 0.4–0.75 L, breathing frequency ranged from 12–22 breaths/min, WOBPHYS/min and WOBN/min ranged from 2.5–12 Joules/min, r = 0.94, r2 = 0.88 (p < 0.05), bias was 0.05 Joule/min, precision was 0.87 Joule/min, and limits of agreement was 1.75 Joule/min. **Conclusions:** WOBN/min obviates the need to measure Pes and was a valid method of estimating WOB during noninvasive PS; it explained 88% of the variance and was an excellent predictor of WOBPHYS/min. WOBN/min may be useful for assessing inspiratory muscles.

## 682

### DEFINING “FLOW STARVATION” IN VOLUME CONTROL MECHANICAL VENTILATION

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**Learning Objectives:** Few studies have assessed the work of breathing (WOB) interaction between an active patient and the ventilator. The term “flow starvation” is used commonly in practice, but has not been objectively defined. We evaluated the relationship between the patient and ventilator inspiratory WOB to define the term “Flow starvation.” **Methods:** A lung simulator (ASL-5000, Ing-Mar Medical Inc.) was programmed as follows: Compliance: 29 mL/cm H2O; Resistance (inspiration): 11 cm H2O/L/s; Resistance (exhalation): 16 cm H2O/L/s. A stepwise increase in patient effort was programmed from an inspiratory muscle pressure (Pmus) of 0 to 25 cm H2O. A mechanical ventilator (Covidien Puritan Bennett 840) was programmed with the following settings: Tidal Volume (VT) 480 mL, frequency 10 breaths/min, constant inspiratory flow: 29 L/min,

inspiratory time: 1 s, and PEEP 11 cm H2O. **Results:** As Pmus increased: VT remained constant (441–448 mL); the average patient WOB increased 32 mJ per cm H2O increase in Pmus; and ventilator WOB decreased correspondingly 28 mJ/cm H2O Pmus. At a Pmus of 15 cm H2O the ventilator WOB is essentially absent. To define flow starvation we measured the peak flow (at peak Pmus) in unassisted breaths at each Pmus step and compared it to the flow delivered by the ventilator at the same point. The difference between ventilator and patient flow (V<sub>vent</sub>–V<sub>pt</sub>) was: Pmus 5 cm H2O: 19 L/m; Pmus 10 cm H2O: 10 L/m; Pmus 15 cm H2O: 1 L/m; Pmus 20 cm H2O: -6 L/m; Pmus 25 cm H2O: -16 L/m. The flow demanded by the patient exceeded the delivered flow above a Pmus of 15 cm H2O, at which point the pressure tracing became negative relative to baseline. **Conclusions:** In volume control ventilation, as the patient inspiratory effort increases, the ventilator WOB decreases, reaching a point where the ventilator no longer assists the patient's WOB. “Flow starvation” occurs when the patient's required flow is higher than that provided by the ventilator. “Flow starvation” is recognized by a drop of the pressure below baseline and occurs at a relatively low Pmus.

## 683

### TISSUE INFLAMMATION IN AWAKE SHEEP SUBJECTED TO EXTRACORPOREAL ACID LOAD CO2 REMOVAL (ALCO2R)

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**Learning Objectives:** ARDS remains a significant medical problem in ICU patients and requires mechanical ventilation which by itself may be injurious. ALCO2R is a unique strategy to reduce ventilator settings to minimize additional lung damage in patients with ARDS. We tested the hypothesis that ALCO2R does not induce an inflammatory response in target organs. **Methods:** Conscious spontaneously breathing sheep (n=6) were connected to a Hemolung (Alung Technologies, Pittsburgh, PA) membrane lung (ML) via heparin-coated tubing and a dual lumen catheter inserted in the right jugular vein. A hemofilter (Purema, Nx Stage Medical, Lawrence, MA) was set up in series after the ML with a pump for recirculation of ultrafiltrate and reinfusion before the ML. 1.5 mEq/min of lactic acid was infused into the ultrafiltrate to acidify blood locally and enhance CO2 removal by the ML. Animals were subjected to ALCO2R or standard CO2 removal without acidification for 12 hr periods twice over a 48 hr period and each sheep served as its own control. Sheep were then euthanized and liver and lungs were flash frozen and analyzed for select indices of oxidative stress and cytokines. **Results:** The efficiency of CO2 removal was 70% higher during ALCO2R than without acid. Cardiac output and oxygen consumption were about 6–8% higher during ALCO2R than without acid. pHa was normal and lactate higher in ALCO2R and markers of kidney and liver function were within the normal range. Lung and liver indices of lipid peroxidation, antioxidant status, as well as glutathione levels and indices of nitrosative stress were similar to historic controls. Lung and liver IL-1β and IL-8 as markers of inflammation were not significantly elevated over the normal range in either tissue. **Conclusions:** Spontaneously breathing sheep subjected to ALCO2R were able to maintain ventilator status with improved efficiency in CO2 removal. Biomarkers of inflammation, oxidant stress and tissue injury suggest that the procedure is safe. Future research will evaluate this technique in an animal model of lung injury. Supported by US Army MRMC.

## 684

### SAFETY AND FEASIBILITY OF PATIENT-CONTROLLED SEDATION (PCS) IN VENTILATED ICU PATIENTS

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**Learning Objectives:** The study aims were to evaluate safety and feasibility of dexmedetomidine patient-controlled sedation (DEX PCS) as a method for patients to self-manage their anxiety for up to 5 days of mechanical ventilation. We hypothesized that mechanically ventilated ICU patients would self-manage their anxiety with DEX PCS safely without serious adverse effects. **Methods:** DEX PCS was administered with a basal infusion (0.1–0.7 mcg/kg/hr) titrated up or down based on patient triggered doses (0.25 mcg/kg/dose, 3/hr max). Dexmedetomidine was delivered through a standard PCA infusion pump with medication syringes prepared at 12 mcg/mL concentration under an FDA IND. Main safety goals were to maintain heart rate > 40 bpm, systolic BP > 80 mm Hg and diastolic > 50 mm Hg. Feasibility was assessed by ability to enroll eligible